

Contents lists available at ScienceDirect

Journal of the American Pharmacists Association

journal homepage: www.japha.org

RESEARCH

The impact of medication reviews by community pharmacists

Ashra Kolhatkar, Lucy Cheng, Fiona K.I. Chan, Mark Harrison, Michael R. Law^{*}

ARTICLE INFO

Article history:

Received 2 February 2016

Accepted 3 May 2016

ABSTRACT

Objectives: Many Canadians use prescription medicines that are unnecessary or that can lead to adverse events. In response, many provinces have introduced programs in which pharmacists are paid to perform medication reviews with patients. As the evidence on such programs is equivocal, we investigated the impact of British Columbia's program.

Design: Interrupted time series.

Setting: British Columbia, Canada.

Participants: All residents of British Columbia who received a medication review between May 1, 2012, and June 30, 2013 (163,776 individuals).

Intervention: Using British Columbia's population-based PharmaNet drug utilization system, we collected data on community pharmacist-led medication reviews. The PharmaNet database contains a record of all medication reviews conducted in an ambulatory setting.

Main outcome measures: We studied the impact of first medication reviews conducted between May 2012 and June 2013. We used interrupted time series analysis to assess longitudinal changes in patients receiving a standard review ($n = 147,770$) and a more intensive pharmacist consultation ($n = 16,006$). Our outcomes included drug utilization, costs, potentially inappropriate prescriptions, and medication persistence measured through the proportion of commonly used chronic medications that were eventually refilled.

Results: Overall, we observed few changes in the level or trend of any of the outcomes we studied. Both review types were followed by significant increases in both the number of prescriptions per month and expenditures. The continuation of long-term medications did not change for 3 of 4 classes, and increased very slightly for the final class. We found no evidence of deprescribing, either for classes that are potentially problematic for long-term use (benzodiazepines and proton pump inhibitors) or for potentially inappropriate prescriptions in seniors.

Conclusions: Our results suggest that medication reviews did not significantly modify prescription drug use by recipients. Future iterations of such programs might be modified to be better targeted and to encourage closer collaboration between pharmacists and prescribing health care professionals.

© 2016 American Pharmacists Association®. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Disclosure: Fiona Chan is employed part-time as a community pharmacist in Vancouver, Canada. Mark Harrison holds the UBC Professorship in Sustainable Health Care, which is funded by Amgen Canada, AstraZeneca Canada, Eli Lilly Canada, GlaxoSmithKline, Merck Canada, Novartis Pharmaceuticals Canada, Pfizer Canada, Boehringer Ingelheim (Canada), Hoffman-La Roche, LifeScan Canada, and Lundbeck Canada. Michael R. Law has consulted for Health Canada on unrelated pharmaceutical policy topics.

Funding: This analysis was funded by a research grant from the Canadian Institute of Health Information. Michael R. Law received salary support through a Canada Research Chair in Access to Medicines and a Michael Smith Foundation for Health Research Scholar Award.

*** Correspondence:** Michael R. Law, PhD, Centre for Health Services and Policy Research, 201-2206 East Mall, Vancouver, BC, V6T 1Z3.

E-mail address: michael.law@ubc.ca (M.R. Law).

Prescription drugs are a fundamental part of modern health care. However, many patients use prescriptions that are unnecessary or lead to adverse outcomes.¹ Canadians take an average of 16 prescriptions every year, and 1 in 8 adults experience adverse drug events from drugs prescribed in ambulatory care settings.^{2,3} Furthermore, estimates suggest that 1 of 9 emergency department visits are related to potentially preventable drug-related adverse events.⁴ These medication issues often arise through complex medication regimens involving multiple prescribers, including both primary care physicians and specialists.^{5,6}

One increasingly popular effort to improve prescription drug use is medication reviews by community pharmacists. A medication review is an individualized, in-person

Key Points**Background:**

- Prescription drug use is often sub-optimal in ambulatory settings, resulting in unnecessary drug use, adverse events, and potentially preventable poor outcomes. Complex medicine regimens and multiple prescribers are related to the risk of adverse drug-related events.
- To address some of these medication-related challenges, many jurisdictions have increased the scope of practice of community-based pharmacists to perform medication reviews. Medication review programs have been implemented internationally, including in 8 of 10 Canadian provinces.
- The existing evidence on the effectiveness of these programs is equivocal.

Findings:

- Between May 2012 and June 2013, pharmacists in the Canadian province of British Columbia conducted nearly 300,000 medication reviews.
- Using a rigorous longitudinal research design, we found no evidence that medication reviews reduced drug costs, improved adherence, or led to the prescribing of potentially inappropriate prescriptions.

appointment in which a pharmacist assesses a patient's current medications, discusses their medications with them, and makes suggestions to optimize their drug therapies. An explicit goal of most medication review programs is to improve patient health outcomes.⁷ A secondary goal is to help patients to consolidate their prescriptions to decrease unnecessary pharmacy visits and encourage patient loyalty to a single pharmacy.⁸ In 2007, Ontario became the first province in Canada to implement a government-sponsored program to compensate community pharmacists for conducting medication reviews for eligible patients.⁹ Since then, 7 other Canadian provinces have implemented similar programs.¹⁰

While the use of medication reviews has increased dramatically, there remains uncertainty regarding their effectiveness.¹¹ One systematic review of interventions targeting adults with uncontrolled hypertension and diabetes found that pharmacist-led medication reviews had beneficial effects on blood pressure and HbA_{1c} glycosylated hemoglobin.¹² However, systematic reviews and randomized controlled trials involving interventions targeted to older people found no effect of these reviews on mortality or hospital admissions.^{13,14} To date, studies of Canadian medication review programs have focused on pharmacist, patient, and physician perceptions of these services.^{15,16} These studies found that while pharmacists believed that their job satisfaction and patient knowledge of medications were positively influenced by medication review programs, there was a negative effect on their workload. Pharmacists also identified a number of barriers to conducting medication reviews, such as lack of time to conduct thorough reviews and inadequate dedicated space to conduct reviews.^{15,16} However, no Canadian studies have quantitatively

measured outcomes such as changes in medicine use and persistence.

Objectives

Despite the equivocal international evidence, the lack of Canadian data, and uncertainty of the impact of medication reviews by community pharmacists, provincial governments in Canada collectively paid more than CAD \$96 million for medication review services in community settings in 2014.^{17,18} Therefore, we studied the impact of the British Columbia medication review program on drug utilization, costs, and medication persistence.

Methods*Study context*

British Columbia (BC) began compensating community pharmacists for performing medication reviews in April 2011. Patients needed to meet at least 1 of several criteria for a clinical need for the service based on the assessment of the pharmacist. From May 2012, eligible patients were required to have been dispensed at least 5 different medications or insulins over the past 6 months. Eligible medications included prescription medications, over-the-counter medications, compounded drug products, and injection drugs.

The BC provincial government funded 3 types of medication review services: standard (MR-S), pharmacist consultation (MR-PC), and follow-up (MR-F). During an MR-S, the patient and pharmacist review the patient's medications to improve their use and understanding of their treatments. The pharmacist prepares a "best possible medication history" for the patient with a list of the medications that the patient can take home with them, and a copy with professional notes that is kept on file and can be sent to another health care provider upon request. If a pharmacist identifies at least 1 drug therapy problem during the review and takes action to resolve it, they may make a claim for an MR-PC instead. An MR-F, available to patients who received an MR-S or MR-PC in the preceding 12 months, is intended to update the patient's best possible medication history following medication changes. Patients were eligible to receive 1 MR-S or MR-PC review in each 6-month period, and may have received up to 4 MR-F reviews in the 12 months following an MR-S or MR-PC. Pharmacists were compensated \$60 for an MR-S, \$70 for an MR-PC, and \$15 for an MR-F.

Data sources and study population

We used the BC PharmaNet system, a population-based administrative database of all prescription drug dispensations in community and hospital outpatient settings in BC.¹⁹ Using PharmaNet, we captured data on individual prescriptions, including drug type, total cost, and the number of units dispensed between December 2010 and June 2014. It also included data on billings for medication review services, including the date and type of medication review that was performed.

Our analyses focused on 2 population-based open cohorts of individuals who received their first medication review between May 1, 2012, and June 30, 2013. The first cohort included

patients whose first review was an MR-S (MR-S cohort, $n = 147,770$), and the second included patients whose first medication review was an MR-PC (MR-PC cohort, $n = 16,006$). We analyzed these groups separately to investigate whether outcomes differed between the different medication review types. Our cohorts excluded patients who received 1 or more medication review before May 1, 2012 ($n = 44,196$), and those whose first recorded medication review was an MR-F ($n = 2870$). To ensure that our cohorts were continuously present in BC during the entire study period, we also excluded patients who did not have at least 1 prescription every 6 months during the study period ($n = 23,933$). For each individual in our final analytic cohorts, we identified their first, or index, medication review and assessed data for the 12 months following this index review.

Measures

We studied the impact of pharmacist medication reviews on a range of outcomes.

Prescription drug use and costs

We calculated the average number of prescriptions dispensed per patient per month. Similarly, we calculated the total expenditure, per capita per month, by all payers over the study period.

Patient medication persistence

To study the impact of medication reviews on patient medication persistence, we calculated the proportion of prescriptions that were refilled—or continued—for several major drug classes. We defined a prescription as *refilled* if the same active ingredient was dispensed again within the days' supply of the original prescription plus 30 days. We studied refills of several evidence-based long-term therapies—statins, diabetes medications, and antihypertensive medications—and 2 classes generally not recommended for long-term use—benzodiazepines and proton pump inhibitors (PPIs).^{20–23} We identified all drugs within these classes using ATC categories.²⁴

Potentially inappropriate prescriptions

To examine whether medication reviews changed potentially problematic prescription drug utilization, we examined the rate of potentially inappropriate prescriptions (PIPs) dispensed to patients aged 65 or older, using Beer's criteria.^{20,21}

Pharmacy use patterns

Finally, we studied the impact of medication reviews on pharmacy visits and loyalty. It was hypothesized by the BC Pharmacy Association that medication reviews could improve the relationship between pharmacists and their clients, leading to an increase in loyalty to a single pharmacy. We calculated the mean number of unique visits to any pharmacy per month per patient, considering all prescriptions filled at the same pharmacy on the same day as 1 visit. To investigate loyalty, we calculated the average number of unique pharmacies visited per patient per month.

Statistical analysis

We explored longitudinal changes in the above outcomes among our 2 cohorts using interrupted time series analysis (ITS), one of the strongest quasi-experimental research designs.²⁵ ITS has been used in many pharmaceutical policy evaluations, including several using the BC PharmaNet datasets.^{26–31} Using ITS, we estimated the change in the level and the trend (i.e., slope) of each outcome following a patient's index medication review. As monthly observations may have been correlated over time, we controlled for autocorrelation using appropriate adjustments for each model in a segmented regression using a generalized least squares model.²⁷ We also conducted sensitivity analyses, which excluded the month of the medication review to account for the impact of many medication reviews being co-timed with prescription refills (results not reported). Please refer to [Appendix 1](#) for a more detailed description of the methods.

Results

Use of medication reviews

Between May 1, 2012, and June 30, 2013, pharmacists conducted 298,319 MR-S and MR-PC medication reviews ([Table 1](#)). MR-S reviews accounted for 89.4% of all reviews, with 266,786 reviews delivered to 147,770 unique patients. MR-PC reviews were used less, with only 31,533 reviews (10.6%) delivered to 16,006 unique patients. More than 57% of recipients of these reviews were female, and almost 47% were age 65 years older. The delivery of these reviews was highly concentrated in particular pharmacies. Ranked by volume of reviews performed, the top 25% of pharmacies accounted for almost three-quarters of all medication reviews performed (72.4%), whereas the bottom 25% accounted for fewer than 2% of medication reviews performed.

Prescription drug use and costs

In the MR-S cohort, the average number of prescriptions per month ranged from 2.91 to 3.98. The average number of prescriptions per patient was higher for the MR-PC cohort (range, 3.47–4.83). We found statistically significant level increases in the number of prescriptions following a patient's first medication review for the MR-PC cohort (0.41 prescriptions per patient [95% CI 0.14–0.68], $P = 0.006$). We found no statistically significant changes in the trend for either cohort following the index medication review.

This increase in prescription drug use corresponded to an increase in total drug expenditure following a patient's first medication review. Total expenditure per patient per month ranged from CAD \$165 to \$191 for the MR-PC cohort, compared to CAD \$142 to \$162 for the MR-S cohort ([Figure 1](#)). We found statistically significant level increases in the total expenditure per capita per month for both cohorts (MR-S, \$7.49 per capita per month [95% CI \$0.41–\$14.6], $P = 0.048$; MR-PC, \$11.98 per capita per month [95% CI \$3.92–\$20.04], $P = 0.007$). We also found statistically significant decreases in the trend for both cohorts following their index medication review (MR-S, $-\$1.27$ per capita per month [95% CI $-\$2.11$ to $-\$0.44$]

Table 1
Descriptive summary of the MR-S and MR-PC cohorts

Patient characteristics	Type 1 (MR-S cohort)	Type 2 (MR-PC cohort)
Total number of reviews	266,786 (89%)	31,533 (11%)
Total number of unique patients	147,770	16,006
Sex		
Male	44%	40%
Female	56%	60%
Mean age (y)	59	63
Percent aged 65 y or older	46%	56%
Number of patients receiving a later review of a different type		
MR-S	—	4463 (30%)
MR-PC	5510 (3.5%)	—
MR-F	16,853 (11%)	4364 (27%)
Percent that submitted claims for one of the following drugs		
Proton pump inhibitors	35%	40%
Statins	46%	49%
Diabetes medications	23%	25%
Benzodiazepines	25%	27%
Anti-hypertensives	68%	73%
Proportion of pharmacies conducting reviews		
Bottom 25%	1.2%	0.9%
Bottom 50%	7.6%	5.0%
Top 25%	73.1%	81.3%

Abbreviations used: MR-S, standard medication review; MR-PC, pharmacists consultation medication review; MR-F, follow-up medication review.

$P = 0.006$; MR-PC, $-\$2.10$ per capita per month [95% CI $-\$3.15$ to $-\$1.04$], $P = 0.001$). In contrast, our sensitivity analysis found no statistically significant changes in either the level (MR-S, $\$3.24$ per capita per month, $P = 0.367$; MR-PC, $\$6.94$ per capita per month, $P = 0.113$) or the trend for either cohort (MR-S, $-\$0.55$ per capita per month, $P = 0.220$; MR-PC, $-\$1.61$ per capita per month, $P = 0.056$).

Patient medication persistence

Our analyses found no change in the continuation of several long-term chronic medications, including diabetes medications and antihypertensives (Table 2). The one exception was statin prescriptions, where we observed a small level increase of 0.52% (95% CI 0.19%–0.86%, $P = 0.005$) in the MR-PC cohort. Similarly, we found no reductions in continuations for PPIs and benzodiazepines. In contrast, we

actually observed a small increase in the trend of refilling benzodiazepines for both cohorts (MR-S, 0.14% per month [95% CI 0.10%–0.19%], $P = 0.001$; MR-PC, 0.34% per month [95% CI 0.20%–0.48%], $P = 0.001$; Figure 2). We also observed an increase in the trend of refilling PPI prescriptions for MR-PC recipients (0.13% per month [95% CI 0.04%–0.21%], $P = 0.007$; Figure 3).

Potentially inappropriate prescriptions

The number of PIPs dispensed per patient increased after the first medication review for patients age 65 years and older (Figure 4). This level change was present in both cohorts (MR-S, 13.32 prescriptions per 1000 patients [95% CI 4.09–22.55], $P = 0.009$; MR-PC, 16.48 prescriptions per 1000 patients [95% CI 1.93–31.02], $P = 0.035$). We found no significant changes in the trend for either cohort.

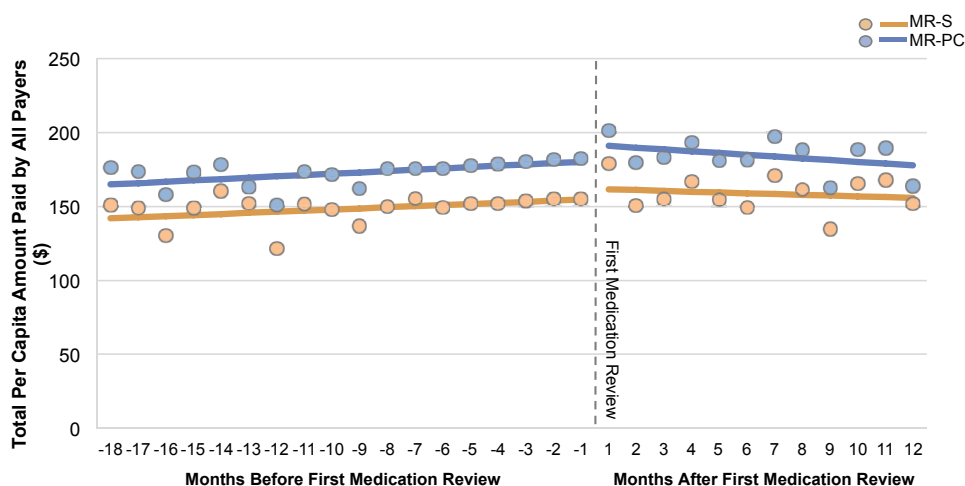


Figure 1. Observed total all-payer spending per capita in British Columbia between May 1, 2012, and June 30, 2013, for patients whose first medication review was an MR-S or an MR-PC (MR-S, $\$7.49$ per capita per month [95% CI $\$0.41$ – $\$14.6$], $P = 0.048$; MR-PC, $\$11.98$ per capita per month [95% CI $\$3.92$ – $\$20.04$], $P = 0.007$).

Table 2

Level and trend changes in the proportion of prescriptions refilled within the days' supply plus 30 days following a first pharmacist medication review

Drug	MR-S				MR-PC			
	Level change (95% CI)	P value	Trend change (95% CI)	P value	Level change (95% CI)	P value	Trend change (95% CI)	P value
Statins	0.39 (−0.66 to 1.45)	0.472	−0.02 (−0.15 to 0.12)	0.815	0.52 (0.19–0.86)	0.005	−0.02 (−0.05 to 0.02)	0.440
Diabetes medications	0.42 (−0.12 to 0.95)	0.142	−0.021 (−0.08 to 0.04)	0.521	0.44 (−0.15 to 1.02)	0.154	0.01 (−0.06 to 0.08)	0.847
Anti-hypertensives	0.15 (−0.69 to 1.00)	0.723	0.01 (−0.01 to 0.11)	0.920	0.04 (−0.40 to 0.49)	0.849	0.03 (−0.03 to 0.09)	0.371
Benzodiazepines	−0.03 (−0.42 to 0.35)	0.867	0.14 (0.10–0.19)	<0.001	0.31 (−0.75 to 1.38)	0.569	0.34 (0.20–0.48)	<0.001
Proton pump inhibitors	0.25 (−0.43 to 0.94)	0.476	0.01 (−0.08 to 0.10)	0.821	0.23 (−0.50 to 0.95)	0.546	0.13 (0.04–0.21)	0.007

MR-S, standard medication review; MR-PC, pharmacists consultation medication review.

Pharmacy use patterns

We found no evidence that medication reviews helped patients consolidate pharmacy visits or increase loyalty to particular pharmacies. For both cohorts, we observed an increase in the number of pharmacy visits per month following the first medication review (MR-S, 0.06 visits per patient [95% CI 0.02–0.10], $P = 0.006$; MR-PC, 0.12 visits per patient [95% CI, 0.07–0.16], $P = 0.001$). We found no change in trend for the MR-S cohort, but there was a trend decrease in the MR-PC cohort (−0.007 pharmacy visits per patient per month [95% CI −0.014 to −0.001], $P = 0.030$).

Counter to the hypothesis that medication reviews would increase loyalty to a particular pharmacy, we found significant level increases in the number of unique pharmacies visited per month following the first medication review for both cohorts (MR-S, 0.018 unique pharmacies per patient [95% CI 0.006–0.030], $P = 0.007$; MR-PC, 0.013 unique pharmacies per patient [95% CI 0.006–0.030], $P = 0.001$). There were also significant decreases in the trend for both cohorts (MR-S, −0.003 unique pharmacies per patient per month [95% CI −0.005 to −0.002], $P = 0.001$; MR-PC, −0.002 unique pharmacies per patient per month [95% CI −0.005 to −0.002], $P = 0.001$). The magnitude of this trend change in both cohorts would have essentially cancelled out the level increase by 1-year post-medication review.

Discussion

Over the past several years, most Canadian provinces have expanded the scope of pharmacy practice to include the provision of medication reviews. In BC, this program has been popular, with more than CAD \$16 million of billings to the provincial government in the 2013–2014 fiscal year.¹⁸ Despite this popularity, we found no meaningful impact of pharmacist medication reviews in BC on overall drug utilization and costs, persistence to several popular medication classes, deprescribing of PIPs, or pharmacy utilization patterns. Although we found that the trend in prescription drug costs decreased slightly post-review in both cohorts, our sensitivity analysis excluding the month of the medication review did not corroborate these findings. This finding suggests that the observed decrease is likely an artifact of patients receiving a review concurrently when they visited the pharmacy to fill a prescription. Taken together, our results suggest that the program did not have an effect on optimizing use of medications and deprescribing inappropriate or unnecessary medications.⁷

Our findings align with prior reviews suggesting limited effectiveness for community pharmacy interventions.¹¹ There are several possible explanations for this. First, for pharmacist recommendations to influence drug utilization, they have to influence physician prescribing; however, evidence suggests that such change is best achieved through direct interaction

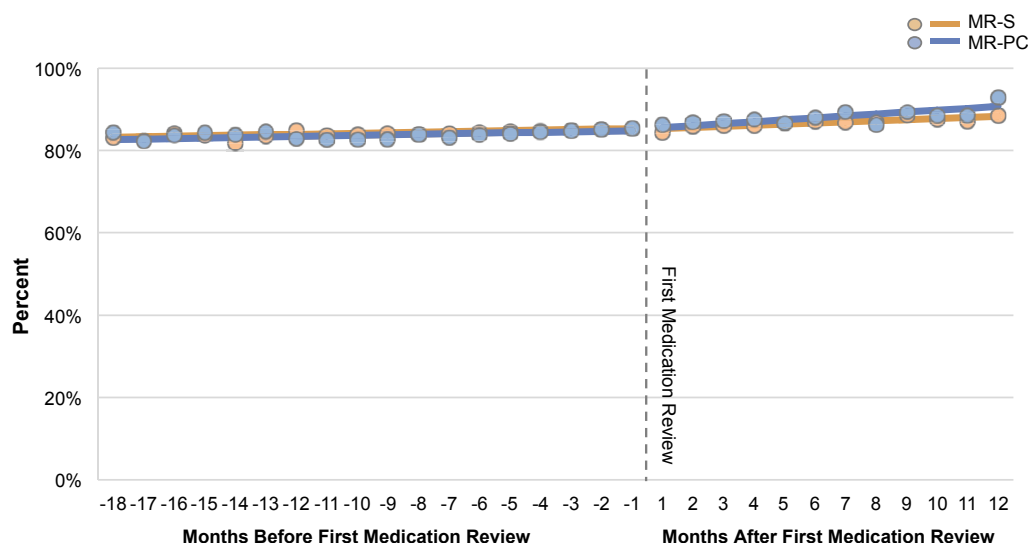


Figure 2. Observed benzodiazepine prescriptions refills within the days' supply plus 30 days in British Columbia between May 1, 2012, and June 30, 2013, for patients whose first medication review was an MR-S or a nMR-PC (MR-S, 0.14% per month [95% CI 0.10%–0.19%], $P = 0.001$; MR-PC, 0.34% per month [95% CI 0.20%–0.48%], $P = 0.001$).

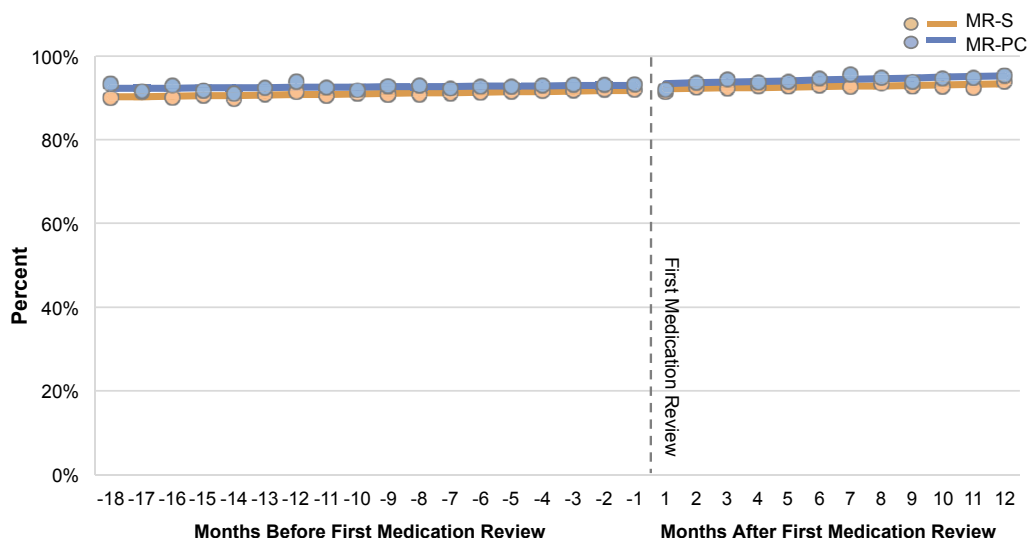


Figure 3. Observed proton pump inhibitor prescription refills within the days' supply plus 30 days in British Columbia between May 1, 2012, and June 30, 2013, for patients whose first medication review was an MR-S or an MR-PC (MR-S, 0.01% per month [95% CI –0.08% to 0.10%], $P = 0.821$; MR-PC, 0.13% per month [95% CI 0.04%–0.21%], $P = 0.007$).

between the pharmacist and prescriber.^{14,32–35} BC medication review guidelines do not require direct contact between the pharmacists and prescribing physicians. Thus, the causal mechanism through which community pharmacists might influence medicine use is much more distal, perhaps explaining the lack of effectiveness we observed.^{36,37} A second factor may be an unwillingness of some physicians to review and act upon documentation sent by pharmacists. A study of a similar program in BC found that physicians believed they were not adequately reimbursed to do so.¹⁶ Additionally, pharmacists might not be correctly or appropriately identifying drug therapy problems, might not be able to make effective changes in response to identified problems, or might not be conducting

effective medication reviews. Finally, pharmacists have reported not having enough time or resources to conduct medication reviews effectively.^{15,16} This may make it more difficult for pharmacists to appropriately target complex patients, for example, who could benefit most from this service. Pharmacists in similar programs have also reported lacking access to relevant and accurate clinical information about their patients, leaving them unable to provide strong recommendations.³⁷ Existing literature, and our study, demonstrate that pharmacist-led interventions targeted at adults with poorly controlled disease states, such as diabetes or hypertension, are more effective than those programs targeted at adults or seniors in general.^{12,13,35}

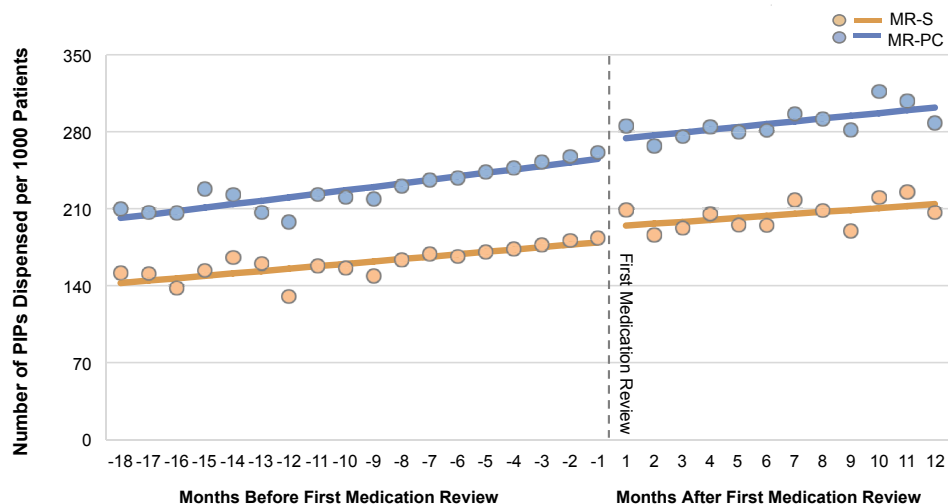


Figure 4. Observed number of potentially inappropriate prescriptions dispensed per 1000 patients in British Columbia between May 1, 2012, and June 30, 2013, for patients whose first medication review was an MR-S or an MR-PC (MR-S, 13.32 prescriptions per 1000 patients [95% CI 4.09–22.55], $P = 0.009$; MR-PC, 16.48 prescriptions per 1000 patients [95% CI 1.93–31.02], $P = 0.035$).

The design, purpose, and goals of medication reviews in BC align closely with medication therapy management (MTM) as defined by the American Pharmacists Association.^{38–41} Many of the shortcomings of the BC medication review program, including limited potential to affect physician prescribing and ineffective or poorly targeted MTM meetings, could arise in MTM services provided by pharmacists across North America. Thus, our findings are relevant to pharmacy practice across Canada and in the United States.

Limitations

The limitations to this study are worth noting. First, we lacked information on actual recommendations that patients received from the pharmacist; therefore, we could not specifically examine their implementation. Second, we have no data on clinical diagnoses for patients, so we are not fully able to assess the appropriateness of particular prescriptions. However, Beer's Criteria are a validated tool and would capture changes in the use of different PIPs over time, as was done in this study.²¹ Third, we did not have any information on medicines received in hospital, as these are not recorded in the PharmaNet database. Fourth, because PharmaNet does not provide information on over-the-counter medications, we were not able to assess the impact of a medication review conducted on the basis of a drug therapy problem related to over-the-counter medication use. Finally, we did not collect or examine data on clinical services use by patients (e.g., emergency department visits, hospitalizations). However, it seems unlikely that health outcomes or clinical services use would have changed in the absence of any observable changes in prescription drug use or persistence.

Conclusions

Our results indicate that medication reviews performed by community pharmacists in BC had little impact, at considerable cost to the provincial government, on the prescription drug use outcomes we examined. While all but 2 provinces in Canada offer these types of medication reviews, this study represents the first quantitative evaluation of these services. Future iterations of medication review programs might consider a more targeted approach. For example, programs could focus on patients who meet multiple criteria of clinical need, are high-cost drug users, or have specific and remediable medication issues. The program could also require contact that is more direct or an existing relationship between pharmacists and patients' prescribing physicians. Overall, our results suggest that medication review programs should be modified and evaluated to ensure value for money in this line of pharmacy services.

Acknowledgments

Data for this study were obtained from the BC PharmaNet system via Population Data BC. All inferences, opinions, and conclusions drawn in this publication are those of the authors, and do not reflect the opinions of Population Data BC or the Data Stewards.

References

- Einerson T. Drug-related hospital admissions. *Ann Pharmacother.* 1992;27(7-8):832–840.
- IMS Health Canada. Prescriptions dispensed in retail pharmacies per capita, by province, 2011. Available at: https://www.imshealth.com/files/ims/Global/North%20America/Canada/Home%20Page%20Content/Press%20Release%20Tables/Top_Pharma_Companies_2011English.pdf. Accessed November 6, 2015.
- Taché SV, Sönnichsen A, Ashcroft DM. Prevalence of adverse drug events in ambulatory care: a systematic review. *Ann Pharmacother.* 2011;45(7-8):977–989.
- Zed PJ, Abu-Laban RB, Balen RM, et al. Incidence, severity and preventability of medication-related visits to the emergency department: a prospective study. *Can Med Assoc J.* 2008;178(12):1563–1569.
- Holmes HM, Luo R, Kuo YF, Baillargeon J, Goodwin JS. Association of potentially inappropriate medication use with patient and prescriber characteristics in Medicare Part D. *Pharmacoepidemiol Drug Saf.* 2013;22:728–734.
- Brown MT, Bussell JK. Medication adherence: WHO cares? *Mayo Clin Proc.* 2011;86(4):304–314.
- Government of British Columbia Pharmaceutical Services Division - Ministry of Health. Pharmacy Fees and Subsidies, and Provider Payment. Available at: <http://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/8-7to8-10.pdf>. Accessed June 6, 2014.
- Boehringer Ingelheim Pharmaceuticals. Unlocking patient satisfaction: 10 keys for pharmacists. Available at: https://www.pharmacysatisfaction.com/resources/pdf/patientresearch/Unlocking%20Patient%20Satisfaction_10%20Keys.pdf. Accessed September 22, 2015.
- Government of Ontario Ministry of Health and long-term care. About MedsCheck. Available at: http://www.health.gov.on.ca/en/public/programs/drugs/medscheck/medscheck_original.aspx. Accessed June 6, 2014.
- Hatah E, Braund R, Tordoff J, Duffull SB. A systematic review and meta-analysis of pharmacist-led fee-for-services medication review. *Br J Clin Pharmacol.* 2013;77(1):102–115.
- Mossialos E, Naci H, Courtin E. Expanding the role of community pharmacists: policymaking in the absence of policy-relevant evidence? *Health Policy.* 2013;111(2):135–148.
- Nkansah N, Mostovetsky O, Yu C, et al. Effect of outpatient pharmacists' non-dispensing roles on patient outcomes and prescribing patterns. *Cochrane Database Syst Rev.* 2010;7:CD000336.
- Holland R, Desborough J, Goodyer L, Hall S, Wright D, Loke YK. Does pharmacist-led medication review help to reduce hospital admissions and deaths in older people? A systematic review and meta-analysis. *Br J Clin Pharmacol.* 2008;65(3):303–316.
- Zermansky AG, Petty DR, Raynor DK, Freemantle N, Vail A, Lowe CJ. Randomised controlled trial of clinical medication review by a pharmacist of elderly patients receiving repeat prescriptions in general practice. *BMJ.* 2001;323(7325):1340.
- Dolovich L, Gagnon A, McAiney CA, Sparrow L, Burns S. Initial pharmacist experience with the Ontario-based MedsCheck program. *Can Pharm J Rev Pharm Can.* 2008;141(6):339–345.e1.
- Henrich N, Tsao N, Gastonguay L, Lynd L, Marra CA. BC Medication management project perspectives of pharmacists, patients and physicians. *Can Pharm J Rev Pharm Can.* 2015;148(2):90–100.
- Canadian Foundation for Pharmacy. Fees and claims data for government sponsored pharmacist services, by province (updated October 2014). Available at: http://www.cfpnet.ca/bank/document_en/75-2013-chart.pdf. Accessed December 18, 2015.
- Government of British Columbia Medical Beneficiary and Pharmaceutical Services Division—British Columbia Ministry of Health. BC Pharmacare newsletter 14-009. 2014 Nov 27;14(009). Available at: <http://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/newsletters/news14-009.pdf>. Accessed September 22, 2015.
- BC Ministry of Health. PharmaNet. Data Extract. Data Stewardship Committee. BC Ministry of Health; 2014. Available at: <http://www.popdata.bc.ca/data>. Accessed June 14, 2016.
- Beers MH, Ouslander JG, Rollingher I, Reuben DB, Brooks J, Bech JC. Explicit criteria for determining inappropriate medication use in nursing home residents. *Arch Intern Med.* 1991;151(9):1825–1832.
- Fick DM, Cooper JW, Wade WE, Waller JL, Maclean JR, Beers MH. Updating the Beers Criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. *Arch Intern Med.* 2003;163(22):2716–2724.
- Janhsen K, Roser P, Hoffman K. The problems of long-term treatment with benzodiazepines and related substances. *Deutsches Arzteblatt Int.* 2015;112:1–7.
- Heidelbaugh JJ, Kim AH, Chang R, Walker PC. Overutilization of proton-pump inhibitors: what the clinician needs to know. *Ther Adv Gastroenterol.* 2012;5(4):219–232.

24. WHO Collaborating Centre for Drug Statistics Methodology, ATC classification index with DDDs, 2015. Oslo 2014. Available at: <http://www.whocc.no/atcddd/>. Accessed July 25, 2014.
25. Wagner AK, Soumerai SB, Zhang F, Ross-Degnan D. Segmented regression analysis of interrupted time series studies in medication use research. *J Clin Pharm Ther*. 2002;27(4):299–309.
26. Grootendorst PV, Dolovich LR, O'Brien BJ, Holbrook AM, Levy AR. Impact of reference-based pricing of nitrates on the use and costs of anti-anginal drugs. *CMAJ*. 2001;165(8):1011–1019.
27. Soumerai S, Ross-Degnan D, Avorn J, McLaughlin T, Chodnoskiy I. Effects of Medicaid drug-payment limits on admission to hospitals and nursing homes. *N Engl J Med*. 1991;325(15):1072–1077.
28. Soumerai SB, Majumdar S, Lipton HL. Evaluating and improving physician prescribing. In: Strom BL, Kimmel SE, Hennessy S, eds. *Pharmacoeconomics*. 5th ed. Hoboken, NJ: Wiley-Blackwell; 2012:402–503.
29. Schneeweiss S, Walker AM, Glynn RJ, Maclure M, Dormuth C, Soumerai SB. Outcomes of reference pricing for angiotensin-converting-enzyme inhibitors. *N Engl J Med*. 2002;346(11):822–829.
30. Tamblin R, Laprise R, Hanley JA, et al. Adverse events associated with prescription drug cost-sharing among poor and elderly persons. *JAMA*. 2001;285(4):421–429.
31. Smalley WE, Griffin MR, Fought RL, Sullivan L, Ray WA. Effect of a prior authorization requirement on the use of nonsteroidal antiinflammatory drugs by Medicaid patients. *N Engl J Med*. 1995;332(24):1612–1617.
32. Gnjidic D, Le Couteur DG, Kouladjian L, Hilmer SN. Deprescribing trials: Methods to reduce polypharmacy and the impact on prescribing and clinical outcomes. *Clin Geriatr Med*. 2012;28(2):237–253.
33. Gnjidic D, Le Couteur DG, Abernethy DR, Hilmer SN. A pilot randomized clinical trial utilizing the drug burden index to reduce exposure to anticholinergic and sedative medications in older people. *Ann Pharmacother*. 2010;44(11):1725–1732.
34. Zarowitz BJ, Stebelsky LA, Muma BK, Romain TM, Peterson EL. Reduction of high-risk polypharmacy drug combinations in patients in a managed care setting. *Pharmacother J Hum Pharmacol Drug Ther*. 2005;25(11):1636–1645.
35. Zermansky AG, Alldred DP, Petty DR, et al. Clinical medication review by a pharmacist of elderly people living in care homes—randomised controlled trial. *Age Ageing*. 2006;35(6):586–591.
36. Freeman CR, Cottrell WN, Kyle G, Williams ID, Nissen L. An evaluation of medication review reports across different settings. *Int J Clin Pharmacol*. 2012;35(1):5–13.
37. Hinchliffe A. *Pharmacist led medication review for older people in the community setting*. Iechyd Cyhoeddus Cymru/Public Health Wales; 2010. Available at: [http://www2.nphs.wales.nhs.uk:8080/PharmaceuticalPHTDocs.nsf/61c1e930f9121fd080256f2a004937ed/f6c649ae73286dc78025779100324aaf/\\$FILE/Literature%20review-%20Pharmacist%20led%20medication%20review%20for%20older%20people%20in%20the%20community%20setting.pdf](http://www2.nphs.wales.nhs.uk:8080/PharmaceuticalPHTDocs.nsf/61c1e930f9121fd080256f2a004937ed/f6c649ae73286dc78025779100324aaf/$FILE/Literature%20review-%20Pharmacist%20led%20medication%20review%20for%20older%20people%20in%20the%20community%20setting.pdf). Accessed September 22, 2015.
38. American Pharmacists Association. APhA MTM Central. Available at: <http://www.pharmacist.com/mtm>. Accessed April 7, 2016.
39. American Pharmacists Association. Medication therapy management services: creating a patient care process for MTM in your practice. American Pharmacists Association; 2007 [cited 2016 Apr 7] p. 1–12. (Creating a Patient Care Process). Report No.: Module 4. Available at: http://www.pharmacist.com/sites/default/files/files/mtm_creating_patient_care_process.pdf. Accessed April 7, 2016.
40. American Pharmacists Association, National Association of Chain Drug Stores Foundation. *Medication therapy management in pharmacy practice: core elements of an MTM service model*. American Pharmacists Association; 2008:1–20. Available at: http://www.pharmacist.com/sites/default/files/files/core_elements_of_an_mtm_practice.pdf. Accessed April 7, 2016.
41. American Pharmacists Association, American Society of Health-System Pharmacists. *Improving care transitions: optimizing medication reconciliation*; March 2012. Available at: http://www.pharmacist.com/sites/default/files/files/2012_improving_care_transitions.pdf. Accessed April 7, 2016.

Ashra Kolhatkar, MPH, Research Coordinator, The Centre for Health Services and Policy Research, School of Population and Public Health, The University of British Columbia, Vancouver, Canada

Lucy Cheng, MSc, Data Analyst, The Centre for Health Services and Policy Research, School of Population and Public Health, The University of British Columbia, Vancouver, Canada

Fiona K.I. Chan, BSc (Pharm), BSPHarm, The Centre for Health Services and Policy Research, School of Population and Public Health, The University of British Columbia, Vancouver, Canada

Mark Harrison, PhD, Assistant Professor, Faculty of Pharmaceutical Sciences, The University of British Columbia, and Centre for Health Evaluation and Outcome Sciences, St. Paul's Hospital, Vancouver, Canada

Michael R. Law, PhD, Canada Research Chair in Access to Medicines, The Centre for Health Services and Policy Research, School of Population and Public Health, The University of British Columbia, Vancouver, Canada

Appendix 1

Generalized least-squares (GLS) regression extends ordinary least-squares estimation of the normal linear model by providing for possibly unequal error variances and for correlations between different errors. A common application of GLS estimation is to time-series regression, in which it is generally implausible to assume that errors are independent. One can detect autocorrelation in time series data, and available statistical software can control for it. For details of application to time series data using the GLS function in the R nlme package, please see Fox and Weisberg (2011).^a

Autocorrelation can be detected visually by inspecting a plot of the residuals over time and by conducting statistical tests (i.e., Durbin-Watson statistics). Randomly scattered residuals

with no discernable pattern indicate no autocorrelation. The *acf* function in the R stats package computes and plots the autocorrelation and partial-autocorrelation functions of a time series. The general pattern of the autocorrelation and partial-autocorrelation functions can be used to specify a model for error autocorrelation.

In our study, a time series is divided into 2 segments separated by an intervention. The first segment includes a series of 18 preintervention observations that establish a baseline trend. The intervention occurs at a known time and then is followed with a series of 12 postintervention observations from which we can analyze the impact of the intervention. The goal is to demonstrate a clear causal relationship between an intervention and an outcome after ruling out other forces that might have had the same outcome in the absence of the intervention.

^a Fox J, Weisberg S. *An R Companion to Applied Regression*, second edition. Thousand Oaks, CA: Sage; 2011.